IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of:		Confirmation No.:	7314
Richard A. PITTNER *et al.*		Art Unit:	1646
Appln. No.:	10/016,969	Examiner:	Ruixiang LI
Filed:	December 14, 2001	Atty. Docket:	18528.010 / 0401-UTL-0
Title:	PEPTIDE YY AND PEPTIDE YY AGONISTS FOR TREATMENT OF METABOLIC DISORDERS		

APPELLANTS' REPLY BRIEF

Mail Stop Appeal Brief – Patent
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

This is a reply to arguments raised in the Examiner's Answer mailed June 13, 2007 ("Examiner's Answer").

In the event that extensions of time beyond those petitioned for herewith are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned. Appellants do not believe any additional fees are due in conjunction with this filing. However, if any fees under 37 C.F.R. §§ 1.16 or 1.17 are required in the present application, including any fees for extensions of time, authorization to charge such fees is given in the accompanying transmittal letter.

REMARKS

1. Introduction

The Examiner's Answer is in response to Appellants' Appeal Brief and Amendment After Final filed February 5, 2007. In the Examiner's Answer, the Examiner entered the Amendment After Final[1], and withdrew the rejections of the claims under 35 U.S.C. § 112, second paragraph and 35 U.S.C. § 102(b). As such, Sections 7(C) and 7(D) of Appellants' Appeal Brief are now moot. However, Claims 33, 43-46, 51, and 54-73 remain rejected under U.S.C. § 112, first paragraph as allegedly lacking enablement and written description. Claim 47 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form.

Appellant's wish to respond to certain arguments raised in the Examiner's Answer with regard to the U.S.C. § 112, first paragraph rejections of the claims.

2. 35 U.S.C. §112, First Paragraph, Enablement

Again, Appellants' respectfully submit that the presently claimed methods are enabled. Applicants have provided ample direction and guidance so as to enable those skilled in the art to practice the recited methods commensurate in scope with the claims.

Again, the claims are directed to novel methods of using a general class of *known* compounds, *i.e.*, PYY agonist analogs.[2] In fact, the Examiner acknowledges that the prior art discloses known PYY agonists, however, not in the context of presently claimed methods. *See, e.g., Examiner's Answer* page 7. Appellants have provided extensive guidance and detail as to the identification of suitable PYY agonist analogs within the scope of general PYY agonist analogs that are useful in the claimed methods. In addition, the claims recite structural and functional elements to clarify the scope of the PYY agonist analogs in this regard. Based on the scope of the claimed compound genus,

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[1] A copy of the presently pending claims following entry of the amendment after final are attached in Appendix A hereto.

[2] Appellants note the discussion in the Examiner's Answer with regard to the scope of general terms "agonist" and "analog" individually. However, the claims recite "PYY agonist analog" within the context of the claimed methods, as well as the structural and functional limitation discussed herein. As such, the scope of the recited PYY compounds are directed to PYY agonist analogs, which are structurally and functionally defined so as to relate to the claimed methods of reducing food intake, appetite, or nutrient availability, weight, weight gain, *etc.*

the teachings of the specification, and the knowledge of those skilled in the art, the skilled artisan would be able to identify PYY agonist analogs that activate Y receptors within the context of the claimed pharmacological effects using only routine experimentation.

Nonetheless, the Examiner's Answer repeatedly asserts that the claims do not provide any structural limitation on the genus of compounds recited in the claims, nor any meaningful functional limitation of the encompassed compounds. Appellants respectfully traverse. The claims recite limitations that clarify the scope of the PYY agonist analogs with regard to structure (*e.g.*, excluding YP as its first two consecutive N-terminal amino acids) and function (*e.g.*, pharmacological effect at various Y receptors greater than PYY[1-36] at a Y1 receptor). As such, the present claims do provide for structural limitation of the recited compound genus, in that PYY agonist analogs are a known genus of compounds that are structurally related to PYY and do not have YP as its first two consecutive N-terminal amino acids. Further, the claims clarify the functional properties of the PYY agonist analogs useful in the claimed methods, in that compounds within the scope of the recited genus exhibit a specific pharmacological effect at particularly Y receptors greater than PYY[1-36] at a Y1 receptor.

The Examiner's Answer also repeatedly asserts that the specification lacks sufficient guidance with regard to screening assays in that there is no disclosure of an assay that involves two varying factors. Again, Applicants respectfully traverse. As recited in the claims and understood by those skilled in the art, such a limitation functionally defines the genus of PYY agonist analogs based on a *single* comparator pharmacological effect, as related across various Y receptor types. The magnitude of a pharmacological effect at a Y receptor may certainly be functionally compared across multiple Y receptor types to functionally define a PYY agonist analog, as recited in the claims.

In this regard, it is noted such comparisons are similar to those that are performed routinely in the art when employing, for instance, positive or negative controls as comparators in scientific studies, both of a clinical as well as a pre-clinical nature. Such comparative control studies are merely run in connection with a test study, and values are

compared. In the present claims, the recited pharmacological effect of PYY[1-36] at Y1 serves as such a comparator, and is compared to the corresponding pharmacological effect that is elicited by a recited PYY agonist analog at a Y2, Y5, or Y7 receptor. Moreover, the specification, and in particular Table 1, is replete with citations to literature comparing the activities of different pancreatic polypeptides at various receptors and for different pharmacological effects. This extensive literature demonstrates that, contrary to the assertions of the Examiner, those skilled in the art are routinely able to compare the effects of PYY molecules at different receptors.

Further, the Examiner's Answer alleges that the pharmacological effect of a test compound on a Y receptor is not an indicator of potency of PYY-related compounds in reducing food intake and gastric emptying. Appellants respectfully traverse. The claims recite that a PYY agonist analog which may be selected in order to practice the claimed methods elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor. In this regard, as disclosed in the subject application, and as noted in Appellants' previous Responses, it has been found that PYY agonist analogs that have a preference for Y2, Y5 or Y7, with less of a preference for Y1, are active in reducing food intake. On the other hand, compounds with a preference for Y1 are not active in reducing food intake. Thus, as the Examiner notes, NPY has a higher potent pharmacological effect on Y1 than PYY[3-36], and is not active in inhibiting food intake. *See Table 1, Specification.*

In sum, based on the teachings in the specification and the knowledge in the art, it is submitted that those skilled in the art would require only routine experimentation to determine which PYY agonist analogs are suitable for use within the context of the claimed methods. For at least these reasons, it is submitted that the claims are sufficiently enabled under 35 U.S.C. § 112, first paragraph, and reversal of this rejection is respectfully requested.

3. 35 U.S.C. §112, First Paragraph, Written Description

Applicants respectfully submit that one skilled in the art would readily appreciate that Applicants, at the time of the filing of the present application, were in possession of

the methods of the claimed invention, including the recited genus and, therefore, have met the written description requirement.

In the Examiner's Answer, the Examiner has cited to *University of Rochester v. Searle* to support the rejection of the claims as lacking written description. Appellants respectfully traverse. The claims in the University of Rochester were directed to the use of a broad class of undisclosed, non-steroidal compounds, limited only by the ultimate functional purpose of inhibiting COX-2. However, no compounds capable of performing in the claimed methods were even disclosed in the University of Rochester patent, let alone exemplified. Rather, as noted by the Examiner, the University of Rochester patent described assays to identify potential compounds, which could include peptides, polynucleotides, and small organic molecules.

Contrasted to the *University of Rochester*, the present specification provides disclosure of a class of generally known peptide compounds (PYY agonist analogs), with specific disclosed examples of compounds which are active in the claimed methods. In addition, the present specification provides detailed guidance as to the identification of which PYY agonist analogs with the general class of PYY agonist analogs have the desired characteristic of reducing food intake, appetite, nutrient availability, weight, weight gain, *etc*. For instance, the specification provides extensive guidance regarding Y receptor preferences (Table 1) and related screening assays (Examples 9 and 10).

Applicants respectfully submit that one skilled in the art would readily appreciate that Applicants, at the time of the filing of the present application, were in possession of the methods of the claimed invention, including the recited genus and, therefore, have met the written description requirement. As such, it is submitted that the claims comply with 35 U.S.C. §112, first paragraph, and reversal of this rejection is respectfully requested.

CONCLUSION

In view of the arguments above, Appellants specifically request that the Board of Patent Appeals and Interferences reverse the Rejections.

Respectfully submitted,

Date: August 10, 2007

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Appendix A: Pending Claims

Claims 1-32. (Canceled)

33. (Previously Presented) The method of any one of claims 43 to 46, 55 to 58, and 64 to 69, wherein the PYY agonist analog has a potency in at least one food intake or gastric emptying assay greater than NPY.

34-42. (Canceled)

43. (Previously Presented) A method of reducing food intake comprising peripherally administering to a human subject, via a parenteral route, an amount of PYY agonist analog effective to reduce food intake, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor, and wherein the amount comprises about 5 μg to 100 μg per day in a single or divided dose.

44. (Previously Presented) A method of reducing food intake comprising peripherally administering to a human subject, via a parenteral route, an amount of a PYY agonist analog effective to reduce food intake, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor, and wherein the amount comprises about 0.1 μg/kg to 10 μg/kg per day in a single or divided dose.

45. (Previously Presented) A method of reducing appetite comprising peripherally administering to a human subject, via a parenteral route, an amount of a PYY agonist analog effective to reduce appetite, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, wherein the

PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor, and wherein the amount comprises about 5 μg to 100 μg per day in a single or divided dose.

46. (Previously Presented) A method of reducing appetite comprising peripherally administering to a human subject, via a parenteral route, an amount of a PYY agonist analog effective to reduce appetite, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor, and wherein the amount comprises about 0.1 μg/kg to 10 μg/kg per day in a single or divided dose.

47. (Previously Presented) The method according to any one of claims 43 to 46, 55 to 58, and 64 to 69, wherein the PYY agonist analog is PYY[3-36].

48-50. (Canceled)

51. (Previously Presented) The method according any one of claims 43 to 46, 55 to 58, and 64 to 69, further comprising administration of a GLP-1, an exendin, an amylin, a leptin, their agonists, or any combination thereof.

52-53. (Canceled)

54. (Previously Presented) The method according to any one of claims 43 to 46, 55 to 58, and 64 to 69, wherein the PYY agonist analog is administered by an intravenous, intraperitoneal, intramuscular, subcutaneous, topical, nasal or pulmonary inhalation route of administration.

55. (Previously Presented) A method of reducing food intake comprising peripherally administering to a human subject who desires to reduce food intake, an amount of a PYY

agonist analog effective to reduce food intake, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

56. (Previously Presented) A method of reducing food intake comprising peripherally administering to a subject in need thereof, via a parenteral route, an amount of a PYY agonist analog effective to reduce food intake, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

57. (Previously Presented) A method of reducing appetite comprising peripherally administering to a subject in need thereof, via a parenteral route, an amount of a PYY agonist analog effective to reduce appetite, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

58. (Previously Presented) A method of reducing nutrient availability comprising peripherally administering to a subject in need thereof, via a parenteral route, an amount of PYY agonist analog effective to reduce nutrient availability, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

59. (Previously Presented) The method according to any one of claims 55 to 58 and 64 to 69 wherein the amount of PYY agonist analog is from about 1 μg to about 5 mg per day in a single or divided doses.

60. (Previously Presented) The method according to any one of claims 55 to 58 and 64 to 69 wherein the amount of PYY agonist analog is from about 5 μg to 100 μg per day in a single or divided doses.

61. (Previously Presented) The method according to any one of claims 55 to 58 and 64 to 69 wherein the amount of PYY agonist analog is from about 0.1 μg/kg to 10 μg/kg per day in a single or divided doses.

62. (Previously Presented) The method according to any one of claims 43 to 46, 55 to 58 and 64 to 69 wherein the PYY agonist analog has a higher affinity for either the Y2 or Y5 receptor than for the Y1 receptor.

63. (Previously Presented) The method of any one of claims 56-58 and 64-69, wherein the subject is a human.

64. (Previously Presented) A method of reducing caloric efficiency comprising peripherally administering to a subject in need thereof, via a parenteral route, an amount of a PYY agonist analog effective to reduce caloric efficiency, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

65. (Previously Presented) A method of reducing food intake comprising peripherally administering to a subject having a condition or disorder which can be treated by reducing food intake, an amount of a PYY agonist analog effective to reduce food intake, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

66. (Previously Presented) A method of reducing nutrient availability comprising peripherally administering to a subject having a condition or disorder which can be treated by reducing nutrient availability, an amount of a PYY agonist analog effective to reduce nutrient availability, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

67. (Previously Presented) A method of reducing appetite comprising peripherally administering to a subject having a condition or disorder which can be treated by reducing appetite, an amount of a PYY agonist analog effective to reduce appetite, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

68. (Previously Presented) A method of reducing weight, reducing weight gain, or increasing weight loss comprising peripherally administering to a subject having a condition or disorder which can be treated by reducing weight, reducing weight gain or increasing weight loss, an amount of a PYY agonist analog effective to reduce weight, reduce weight, reduce weight gain or increase weight loss, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino acids, and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

69. (Previously Presented) A method of reducing food intake and body weight comprising peripherally administering to a subject having a condition or disorder which can be treated by reducing food intake and body weight, an amount of a PYY agonist analog effective to reduce food intake and body weight, wherein the PYY agonist analog is a peptide which does not comprise YP as its first two consecutive N-terminal amino

acids, and wherein the PYY agonist analog elicits a pharmacological effect at a Y2, Y5 or Y7 receptor greater than that of PYY[1-36] at a Y1 receptor.

70. (Previously Presented) The method of any one of claims 64-69, wherein the disorder is an eating disorder, a reproductive disorder, obesity, insulin-resistance, hypertension, atherosclerosis, dyslipidemia, cardiovascular risk, stroke, congestive heart failure, gallbladder disease, osteoarthritis, sleep apnea, or diabetes mellitus of any kind.

71. (Previously Presented) The method of any one of claims 43-46, 55-58, and 64-69, wherein the PYY agonist analog activates a Y2 or Y5 receptor greater than a Y1 receptor.

72. (Previously Presented) The method of any one of claims 43-46, 55-58, and 64-69, wherein the PYY agonist analog elicits a pharmacological effect at a Y7 receptor greater than that of NPY.

73. (Previously Presented) The method of any one of claims 43-46, 55-58, and 64-69, wherein the pharmacological effect at the Y1 receptor is an increase in blood pressure.

74. (Canceled)